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50. (Amended) A plasmid comprising a gene according to claim 1 which is adapted to integrate into a specific attachment site (att) of a host's chromosome.

52. (Amended) A method of producing a transformant microorganism comprising the steps of:

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- (a) producing a plasmid which comprises donor DNA which encodes at least one domain of a first type I PKS;
  - (b) transforming with said plasmid an organism having a chromosome including PKS genes comprising at least one second type I PKS gene which is heterologous to said first PKS, under conditions causing integration of said donor DNA into the chromosome so as to form with a portion of said second type I PKS gene a hybrid PKS gene encoding at least one domain of said first type I PKS and at least one domain of said second type I PKS.

53. (Amended) A method according to claim 51, wherein said plasmid is adapted to integrate into a specific att site of said chromosome, said plasmid being integrated into said chromosome at a location suitable for producing said hybrid PKS gene.

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54. (Amended) A hybrid PKS gene according to claim 1, wherein said first type I PKS naturally includes a thioesterase as

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cont

~~a chain terminating enzyme, and wherein said hybrid gene includes a nucleic acid sequence encoding the enzyme from the rapamycin system which, in said rapamycin system, effects connection of the polyketide chain to an amino acid chain in place of said thioesterase.~~

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Add new claims 59-63 as follows:

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59. (New) A method according to claim 39 wherein said actinomycete is selected from the group consisting of:

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Saccharopolyspora erythraea, Streptomyces coelicolor, Streptomyces avermitilis, Streptomyces griseofuscus, Streptomyces cinnamonensis, Micromonospora griseorubida, Streptomyces hygroscopicus, Streptomyces fradiae, Streptomyces longisporoflavus, Streptomyces lasaliensis, Streptomyces tsukubaensis, Streptomyces griseus, Streptomyces venezuelae, Streptomyces antibioticus, Streptomyces lividans, Streptomyces rimosus and Streptomyces albus.

60. (New) A method according to claim 39, wherein said actinomycete is a Streptomyces.

61. (New) A hybrid polyketide synthase ("PKS") gene comprising a plurality of modules in which a DNA portion encoding a combinatorial module has been replaced by a DNA portion

encoding at lease one equivalent heterologous combinatorial module, said combinatorial module being a contiguous polypeptide sequence extending from a first point in one module to a second point at the corresponding position in the next module.

62. (New) A hybrid polyketide synthase ("PKS") gene produced by
- (a) providing a first nucleic acid portion encoding a plurality of modules of a first typeI PKS including a first extension module which is adapted to produce a ketide unit of a first type; and
  - (b) replacing the nucleic acid encoding said first extension module with a second nucleic acid portion encoding a second extension module which is effective to produce a ketide unit of a second type, differing from said first type in at least one of the characteristics selected from the group consisting of oxidation state, stereochemistry and substitution pattern.

63. (New) A hybrid polyketide synthase (PKS) gene comprising:
- (a) a first nucleic acid portion of a first typeI PKS, said portion encoding a loading module and only the ketosynthase (KS) domain of the extension module which is homologous to said loading module; and
  - (b) a second nucleic acid portion of a second typeI PKS comprising nucleic acid encoding a partial extension module